

**Claims**

*Sub D1*  
1. A modified extracellular domain of a cytokine receptor protein, capable of being  
5 crystallized without being complexed to a ligand molecule.

*Sub E5*  
2. A modified protein according to claim 1 being a homo- or heterodimeric cytokine  
receptor.

*A* 10 3. A modified protein according to ~~claims 1 or 2~~ wherein at least one molecule  
segment which contributes to a disordered structure is deleted.

*Sub D2*  
4. A modified protein according to claim 3 truncated in at least one terminal end.

*Sub E15*  
5. A modified protein according to claim 4 truncated in its C-terminal end and in its  
N-terminal end.

*Sub D3*  
6. A modified protein according to claim 5 being human growth hormone receptor  
(hGHR).

*A* 20 7. A modified human growth hormone receptor (hGHR) according to claim 6 having  
31 or 33 amino acid residues removed in its N-terminal end.

*A* 25 8. A modified human growth hormone receptor (hGHR) according to claim 6 or 7  
having 3 or 4 amino acid residues removed in its C-terminal end.

*Sub A1*  
9. A modified human growth hormone receptor (hGHR) according to any of claims 6  
to 8 consisting of residues 32-237, 32-234 or 34-233 of the native molecule.

*Sub D30*  
10. A modified human growth hormone receptor (hGHR) according to claim 9  
consisting of residues 32-237 of the native molecule.

*Sub A2*

11. Crystals of a receptor protein according to any of claims 1 to 10 to any of claims 1-10 suitable for binding studies with ligand candidates.

5 12. Crystals according to claim 11, wherein the contact surface between two molecules is between 200 to 1800 Å<sup>2</sup> (square ångström) and more preferably between 100 to 900 Å<sup>2</sup> (square ångström)

10 13. Crystals according to claim 11 or 12 containing at least 50 % (v/v) of a solvent acceptable for binding studies.

14. Crystals according to claim 13 containing about 60 to 80 % (v/v) of a solvent.

15 15. Crystals according to any of claims 11 to 14 capable of being frozen with gaseous or liquid nitrogen with maintained capacity of diffraction to at least 3.5 Å by using synchrotron radiation source.

20 16. Crystals according to claim 15 capable of being frozen with gaseous or liquid nitrogen with maintained capacity of diffraction to at least 3.5 Å by using synchrotron radiation source.

25 17. Crystals according to any of claims 11 to 16 capable of being resistant to an addition of up to 10% (v/v) of DMSO (dimethylsulfoxide) and up to 5 % (v/v) of DMF (dimethylfluoride) for at least 24 hours.

18. Crystals according to any of claims 11 to 17 characterized in that they are formed at pH between 5.0 to 8.5.

30 19. Crystals according to claim 18 characterized in that they are formed at a pH between 7.0 and 8.0

20. Crystals according to any of claims 11 to 17 formed in the presence of one or more salts having a concentration between 0.15 M and 1.0 M.

21. Crystals according to claim 20, wherein the salt(s) is(are) selected from a group 5 consisting of ammonium sulfate, lithium sulfate, sodium phosphate, potassium phosphate, sodium chloride, lithium chloride, ammonium acetate, sodium acetate, magnesium chloride, sodium formate and sodium citrate.

22. A method of designing drugs with cytokine receptor activity by employing the 10 crystals according to ~~any of claims 11 to 21~~ <sup>claim 11</sup> in binding studies with selected ligand candidates.

23. A method according to claim 22 involving dimerization of the receptor.

15 24. A method according to claims 22 or 23, wherein the crystals are soaked or co-crystallized with a solution comprising the ligands.

20 25. A method according to any claims 22 to 24, wherein the receptor is a modified growth hormone receptor investigated with ligands having potential growth hormone activity.

26. A method of obtaining improved cytokine receptor crystals involving the subsequent steps of:

(i) solving the receptor three-dimensional structure complexed to a ligand by 25 crystallographic methods,

(ii) identifying regions of the receptor molecule which may contribute to disorder in a crystalline state,

(iii) producing modified receptor molecules without said regions, and

(iv) crystallizing the modified receptor without the presence of a ligand.

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27. A method according to claim 26 involving the extracellular part of the receptor.

*A*

28. A method according to claim 26 or 27, wherein said receptor is human growth hormone receptor.

5 29. A method according to claim 28, wherein said ligand is human growth hormone.

*Add C1*  *Add S2*